ABSTRACT

Background

Myelin basic protein (MBP), a crucial neuro-autoantigen involved in the maintenance of the myelin sheath, is one of the biomarkers of therapeutic response in multiple sclerosis (MS). This neuroinflammatory autoimmune disease might result from molecular mimicry of MBP. The present study examines its role as a prognostic biomarker and evaluates the molecular mimicry hypothesis of MS etiology by using MBP to induce the immune system. MBP was used at varying concentrations to assess the optimum concentration of the antigen required to induce cellular immunity and to understand its prognostic value to facilitate early diagnosis in MS.

Method

A novel methodology combining molecular techniques was used to confirm the antigenic properties of MBP and study its efficiency in increasing the susceptibility to MS. Three groups of thirty subjects each, untreated MS, untreated MS with and without family history, and untreated MS at two different time points from diagnosis (early: 1-15 and late: 15-23 days) were recruited for the study. Healthy individuals were recruited to serve as controls. Peripheral blood mononuclear cells (PBMCs) and plasma was used for the retrieval of MBP and IgG assay, respectively.

We used a novel *in silico* procedure to select antigenic MBP sequences based on T-cell and B-cell predictions, conserved selected epitopes, multiple alignment, and BLASTP ClustalW for presenting the motifs common to all six human MBP isoforms. Then, experiments were conducted by the slope line derived from the measured IgG serum levels in untreated MS patients and healthy individuals against the MBP epitope of untreated MS patients and healthy individuals.

Results

The optimum concentration of the MBP epitope for the immune system to react and facilitate prognostication was found to be 50 and 150 μg/mL in MS patients and healthy individuals, respectively. Combined results from ELISA and real-time PCR showed that the total IgG and the ratio of gene expression for candidate human MBP epitope was higher in MS patients in all the three groups compared to that in healthy controls.

By performing a bioinformatics analysis starting with common epitopic fragments for classic and non-classic MBP isoforms, we predicted four epitopic regions of human MBP sequences based on antigenic priority: 110–124, 7–21, 38–52, and 156–170. The collections of viral and bacterial protein families with 100% pattern- similarity exhibited cross-reactivity between MBP epitopes and 15 proteins in 16 bacteria and 39 proteins in 43 viruses. IgG assay revealed that the concentration of IgG in healthy controls was less than that in patients.

Conclusions

Molecular assays in the early stages of the disease could help in elucidating the effectiveness of the MBP as a prognostic factor in MS. Future research in the field of biomarker detection for MS would benefit from a targeted approach that would enhance accuracy, be economical, and provide leads for the development of the personalized treatment for MS.

The predicted candidate MBP epitope confirmed stimulation of the immune system by increasing total IgG in patient sera. The results suggest that bioinformatics can guide *in vitro* work. Future research on autoantigenic targets of the central nervous system in combination with precise experimental observations might explain MS etiology and facilitate individualized treatments.

Keywords: Multiple sclerosis; Myelin basic protein; Epitope prediction; Molecular mimicry,Biomarker